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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,707	10/27/2005	Masataka Kuwana	4439-4036	2198

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EXAMINER	
DUTT, ADITI	

ART UNIT	PAPER NUMBER
1649	

NOTIFICATION DATE	DELIVERY MODE
07/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ptopatentcommunication@lockelord.com

Office Action Summary	Application No.	Applicant(s)	
	10/549,707	KUWANA ET AL.	
	Examiner	Art Unit	
	Aditi Dutt	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-16,19,20 and 22* is/are pending in the application.

4a) Of the above claim(s) *9-16,19,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 April 2009 has been entered.

Status of Claims

2. The amendment filed on 23 April 2009 has been entered into the record and has been fully considered.

3. Claim 2 is amended. Claims 9-16, 19-20 and 22, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

4. Claims 2-8, drawn to a monocyte-derived multipotent cell (MOMC) expressing CD14, CD34, CD45, type I collagen, and HLA-DR, are under consideration in the instant application.

Response to Amendment

5. Upon consideration of the Applicant's amendment, all claim objections and rejections, not reiterated herein have been withdrawn, as overcome by cancellation and/or amendment of claims (23 April 2009).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 2-8 are rejected under 35 U.S.C. 102(b) as clearly anticipated by Zhao et al., (PNAS 100: 2426-2431, 2003).

7. The claims are directed to a monocyte-derived multipotent cell (MOMC) that expresses CD14, CD34, CD45, type I collagen, and HLA-DR, wherein the cell differentiates into osteoblast, skeletal myoblast, chondrocytes, adipocytes, neurons, endothelial cells and mesodermal cells.

8. Zhao et al. teach the isolation of pluripotent stem cells from human peripheral blood monocytes that resemble fibroblasts and express the monocytic and hematopoietic cellular differentiation stem cell markers, such as CD14, CD34

and CD45 and HLA-DR (pages 2427-2428, Table 1). Zhao et al. further teach that human peripheral blood cells containing monocytes, when cultured under specific conditions, differentiate into macrophages, lymphocytes, epithelial, neuronal, endothelial and hepatocytes etc. (pages 2428-2430). However, as evidenced in Stem Cells (NIH, June 2001, pages 32-35), monocytes, macrophages, lymphocytes etc., are cells that belong to the mesenchymal or mesodermal family and, therefore, this limitation is inherent in the teachings of Zhao et al. Furthermore, although the reference is silent on the expression of collagen type I, this would be an inherent characteristic because the cells are derived from monocytes isolated from the peripheral blood mononuclear cells. Thus, Zhao et al. clearly anticipate the claimed invention.

Applicant's Response:

9. Applicant disagrees with Examiner's reasoning and conclusion in rejecting the claims. Specifically Applicant argues that the Zhao cells are different from MOMC by laying emphasis on essentially two issues: (i) The f-MΦ or the PSC cells of Zhao exhibit reduced levels of HLA-DR (Table 1), while the instant specification demonstrates a very high expression of the same, as indicated by "++" (Example 20, Table 2). Applicant thereby argues that while HLA-DR is negative for PSC, it is positive for the instantly claimed MOMC. Applicant amended claim 2 reciting the additional marker HLA-DR. (ii) Zhao cells "hardly

proliferate" in the absence of the M-CSF treatment, while the MOMC cells do not require M-CSF for proliferation. Based on these findings, Applicant asserts that the prior art cells are undisputedly different from MOMC, adding that "to argue otherwise, is to ignore the critical elements in functional characterization of MOMC and PSC cells". Lastly, Applicant disagrees that PSC cells must be reproduced "in order to conduct a proper comparison", further alleging that Examiner's conclusion is without merit. Applicant argues that the Zhao results were relied as being true, and compared with the findings corresponding to MOMC as presented in the instant disclosure and in the Kuwana declaration. As per Dr. Kuwana's declaration dated 20 August 2008, attempts to induce MOMC with different factors used by Zhao, e.g. IL-2 factor, nerve growth factor or epidermal growth factor, for differentiation to T-cells, neuronal cells and epithelial cells, respectively as shown by Zhao, resulted in failure, thereby proving that a person skilled in the art "could and would deduce that MOMCs are distinct from PSCs". Applicants, therefore, conclude that the PSC of Zhao is distinct from the claimed MOMC, and that Zhao does not anticipate the claimed invention. Also because Zhao does not disclose each and every element of the claims, Applicants request reconsideration and withdrawal of the rejection.

10. Applicant's arguments are fully considered, however, are not found to be persuasive. Firstly, contrary to Applicant's allegation, Zhao cells do not show a negative staining for HLA-DR, rather a reduced expression for the marker than s-MΦ (see Table 1). Additionally, Applicant's contention that the instant

specification demonstrates a "very high" expression or a "strong staining" of HLA-DR is not quite evident and expressly disclosed. Page 38 (paragraph 1) of the specification teaches that HLA-DR is expressed on MOMC, however, the disclosure neither states a strong or a weak expression, nor defines a "++" indication in Table 2, as describing such degree of staining. Besides, arguments that rely on particular distinguishing features are not persuasive when those features are not recited in the claims. In the present situation, there is no requirement for a high or low expression of HLA-DR. The claims only require that the cells express HLA-DR. While the claims are to be interpreted in light of the specification, it does not follow that limitations from the specification may be read into claims. On the contrary, claims must be interpreted as broadly as their terms reasonably allow. See Ex parte Oetiker, 23 USPQ2d 1641 (BPAI, 1992). Applicant is reminded that the claims define the subject matter of his invention and that the specification cannot be relied upon to read limitations into the claims.

11. With regards to Applicant's arguments that the Zhao cells require M-CSF to elicit proliferation, while MOMC do not require this factor, Applicant is again reminded as stated in the previous Office Action that the claim recites a product by process. As set forth in MPEP Chapter 2113, "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process

claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985). Furthermore, the alleged feature (whether or not the cells require M-CSF in order to proliferate) is not recited in the claims. What is claimed is a cell that is multipotent and derived from a monocyte, that expresses CD14, CD34, CD45, type I collagen, and HLA-DR, can differentiate into several recited cell types, and can be obtained by culturing certain blood cells and collecting cells that look like fibroblasts. What is taught by Zhao is a cell that is multipotent and derived from a monocyte, that expresses CD14, CD34, CD45, and HLA-DR, can differentiate into several cell types, and can be obtained by culturing certain blood cells and collecting cells that look like fibroblasts.

12. Therefore, product-by-process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps. As explained earlier, the method steps recited in the instant claims neither relate to the claimed multipotent cells, nor imply any structural limitations to the product. Besides, the argument is moot since the M-CSF limitation is not even recited in the instant claims. That MOMC and PSC cells are derived from the same source, are structurally similar and express the same markers as claimed, and additionally are multipotent or pluripotent stem cells having the potential of differentiation to various cell lineages go on to prove that the critical elements in functional

characterization of the prior art cells and the cells of the instant invention are identical.

13. With regards to Applicant's disagreement over Examiner's requirement for more conclusive information in comparison to the Zhao data, it is clarified that Applicant is not required to reproduce the PSC cells of Zhao. Applicants have argued that they were not able to follow the protocol of Zhao, but have not presented evidence that the claimed invention – MOMC, is different from that of Zhao - PSC. As stated above, it is reiterated that the claims represent a product by process, and the patentability of the claimed product does not depend on the process of making the product. It is noted that "The Patent Office bears a lesser burden of proof in making out a case of *prima facie* obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. *In re Fessmann,* 489 F.2d 742, 744, 180 USPQ 324, 326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi,* 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983) (MPEP 2113). In this case the Office has set forth a prima facie case of inherency with respect to the product-by-process claims based on extensive reasoning provided above. As such "[T]he PTO can require

an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his [or her] claimed product (MPEP 2112 V). The purpose here is not to prove whether the Zhao findings are true or not, but to compare MOMC with PSC. Applicant did not present a comprehensive data, based on which one skilled in the art can determine that PSC is different from MOMC.

14. Furthermore, Applicant's failure to achieve differentiation again goes on to prove the Blau and Seta teachings as stated in the previous Office Action dated 16 December 2008, page 6-7, para 11. Specifically, cellular differentiation can also depend on culture conditions and environmental cues, thereby indicating a dynamic feature. For example, Seta et al. teach that "distinct differentiation potentials of these primitive cells might be due to different culture conditions of the same precursors" (primitive cells correspond to monocyte derived cells) (page 46, para 1). This corroborates with the Blau statement that adult stem cells and progenitor cells are not unique and compartmentalized to differentiation to specific cell types expressing specific markers. Blau et al further teach that stem cells can give rise to various cell lineages and tissues depending on the microenvironmental cues, growth factors, differentiation factors, etc., by virtue of plasticity, heterogeneity and transdifferentiation characteristics (Figs 1, 7, 8). For example neural stem cells can form skeletal muscle, bone marrow derived stem cells can form multiple tissues, and cells from various tissues can give rise to bone marrow cells (page 837, para 1). Hence PSC of Zhao et al and the instant

MOMC, both being multipotent or pluripotent stem cells, both having derived from the same source and expressing the same markers, have similar differentiation potential based upon the Blau teaching.

15. For reasons explained above, Zhao's PSC are structurally the same as MOMC, therefore, the cells of the prior art would be functionally the same under identical culture conditions, absent evidence to contrary.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aditi Dutt whose telephone number is (571) 272-9037. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:00 p.m.

18. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

19. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-

direct.uspto.gov/. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

AD
12 July 2009

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
July 16, 2009